REMARKS

Claims 4-9 and 12-17 are active in the present application.

The rejection of Claims 4-9 and 12-17 under 35 U.S.C. §112, first paragraph (enablement), is traversed.

The Office has taken the position that the claimed invention is not supported by an enabling disclosure (paper number 7, paragraph bridging pages 2 and 3). Applicants respectfully disagree.

At the outset, Applicants wish to make the following comments regarding the references which the Examiner cites in support of the rejection.

In regard to Marechal et al (Physiologia Plantarium, 1997, 100(1), 65-77), Applicants note very little is known about the enzymes that catalyze glycerolipid biosynthesis in higher plants (page 66, left column, first full paragraph). Accordingly, the authors wanted to explain that compared with the understanding of enzymes involved in fatty acid biosynthesis and desaturation, very little is known *at the molecular level* about the enzymes that catalyze glycerolipid biosynthesis, specifying later the assembly of the three parts of a glycerolipid molecule.

In addition, while MGDG synthase represents only a minor envelope protein in terms of the overall proportion, this enzyme catalyze the synthesis of a product (MGDG) that is perhaps the most abundant polar lipid on earth due to its near ubiquitous presence in the most widely developed membrane system, thylakoids (page 67, left column, end of first paragraph) and others, as shown on Figure 1 in page 66.

Moreover, the Applicants disagree with the Examiner's interpretation of Figure 2B in Miege et al (Plant Physiol. Biochem., 1999, 37 (11), 795-808). Indeed, whether different

known pathways and enzymes are involved in the conversion of the intermediate DAG to membrane glycerolipids, it appears that each of these pathways lead to the production of specific glycerolipids and in particular there is no enzyme synthesizing MGDG other than MGDG synthase. Accordingly, *there is no alternative pathway or enzyme* other than MGDG synthase leading to MGDG generation.

Furthermore, the Examiner asserts based on page 798, paragraph 1 of Miege et al that the function of MGDG enzyme *in vivo* is still a matter of debate. However, the enzyme that is concerned in such a debate is *not* MGDG synthase, but rather is the enzyme involved in an activity from the outer membrane of the plastid envelope that is able to generate DAG *in vitro*, by transferring a galactosyl residue from a MGDG molecule to another generating DGDG as disclosed in the preceding sentence of the paragraph and identified as "GGGT" in Figure 2B.

The question that the Examiner should ask when evaluating enablement is set forth in MPEP § 2164.01, which states:

> The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.

Applicants submit that the artisan would well appreciate how to practice the claimed method when the knowledge generally available in the art is couple with the disclosure of the present application.

The present invention provides, in part, a method for screening and for selecting antiparasitic agents, herbicides or combinations thereof, comprising

-incubating a substance to be tested with an MGDG synthase or with a plastidial membrane isolated from a plant, and

-measuring the specific enzymatic activity, after said incubation (see Claim 1).

The present invention also provides pharmaceutical compositions comprising MGDG

synthase inhibitors (Claim 12) or compounds identified from the method above (Claim 15).

Surely, the Examiner must recognize that the level of skill in the art to which the invention pertains is sufficient to screen candidate compounds by incubating the same with an MGDG synthase or with a plastidial membrane isolated from a plant, and measuring the specific enzymatic activity resulting therefrom.

Further, as clearly set forth in the specification, the present invention flows from the identification of plastid-like structures in *Toxoplasma* and *Plasmodium* and the key role of MGDG into the biogenesis of plastids and cell survival in higher plants. Accordingly, the present invention is related to the use of MGDG synthase (*i.e.* the enzyme responsible of the biosynthesis of MGDG) for selecting or screening inhibitors of MGDG synthase activity. The MGDG synthase inhibitors identified thereby may then be used as antiparasitic agents and/or herbicides. Therefore, the underlying theme of the present invention is the relation between parasites and higher plants (and consequently between antiparasitic and herbicide activities) is the presence of plastids.

In the Office Action, the Examiner questions the adequacy of the evidentiary correlation between MGDG synthase, detection thereof, and its use for identifying antiparasitic agents. To this end, Applicants **submit herewith** a Declaration under 37 C.F.R. §1.132 executed by Mr. Eric Marechal (the Marechal Declaration). In the Marechal Declaration, the inventors have demonstrated that the plastid-like structures in *Toxoplasma* and *Plasmodium* contain a functional MGDG synthase flowing from the detection of MGDG in *Toxoplasma gondii* (see the results of the Marechal Declaration).

As set forth in the "Conclusion" of the Marechal Declaration, the evidence contained therein clearly demonstrates the presence of MGDG in an apicomplex parasite, *Toxoplasma gondii* and that, consequently, the MGDG synthase which serves as a target to search or a

molecule with antiparasitic properties according to the present invention clearly exists in apicomplex parasites. Therefore, the Marechal Declaration confirms that one of the possible applications of the search for inhibitors of plant MGDG synthase is the identification of anti-apicomplex parasite agents.

In view of the foregoing, Applicants request withdrawal of this ground of rejection.

The rejection of Claims 12-17 under 35 U.S.C. §112, second paragraph, is traversed.

The Examiner has objected to the phrase "pharmaceutical composition comprising a MGDG synthase inhibitor." The Examiner contends that the meaning of this term is unclear. Applicants note that the plain meaning of the claims readily establishes the fact that the composition contains an MGDG synthase inhibitor and a pharmaceutically-acceptable carrier or excipient. Moreover, the specification at page 5, lines 7-9, clearly states "inhibition of the enzymatic activity is defined by a decrease in the activity of at least 50%, as a percentage for control activity." Therefore, the artisan would readily appreciate that the identity of the MGDG synthase inhibitor identified by the claimed method and/or falling within the scope of Claim 12 would satisfy the definition provided in the specification for the same.

Applicants remind the Examiner that: "Applicants are their own lexicographer." Accordingly, as dictated by MPEP §2173.02, the Examiner should ask whether the term is adequately defined in the specification so as to enable the artisan to appreciate the meaning of the term. Based on the disclosure in the specification discussed above, Applicants submit that the skilled artisan would readily appreciate the nature of the MGDG synthase inhibitor. Accordingly, Applicants submit that this term is definite within the context of 35 U.S.C. §112, second paragraph.

Furthermore, Applicants submit that the explanation provided above, which has been augmented by the Marechal Declaration, clarify the relationship between screening and selecting antiparasitic agents and/or herbicides and a MGDG synthase inhibitor for use in a pharmaceutical composition for treating an animal having an apicomplex parasite and/or use as herbicide.

Therefore, in view of the foregoing, Applicants request withdrawal of this ground of rejection.

Applicants submit that the present application is now in condition for allowance. Early notification of such action is earnestly solicited.

Respectfully submitted,

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